CHEMICAL TRANSFORMATIONS OF DIOLS AND CYCLIC ETHERS. XXXIV*

Mechanism of Reactions of Diols with Acid Chlorides

By

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A study was made of the mechanism of reactions of diols with acetyl chloride, and mainly the second step of the process, the substitution of the hydroxy groups of the monoacetates by chlorine. It was found that, similarly to the 1,2-diol monoacetates, the di-primary and primary-secondary 1,3-diol monoacetates react *via* a cyclic acetoxonium transition state. The monoacetates of the 1,4-diols react with HCl by S_N2 reactions. This indicates that under the conditions used no seven-membered cyclic acetoxonium cation is formed. Hence, the fact that in acidic medium intramolecular acyl migration occurs for the 1,4-diol monoacetates is a new evidence in support of a mechanism for the acyl migration involving a cyclic transition state.

Introduction

In an earlier paper [1], our studies in connection with the reactions of various diols with acetyl chloride and benzoyl chloride were described. The course of the first step of the process, the formation of the diol monoester was examined. In the present paper the examination is extended to the second step of the process, the exchange of the hydroxy groups of the monoacetates for chlorine. Our earlier studies showed that in the formation of the chloroacetates the 1,2- and the 1,3-diols behave similarly in the case of both the di-primary and the primary-secondary diols, but there is a fundamental difference between the 1,3- and the 1,4-diols. For this reason butane-1,3-diol and pentane-1,4-diol were selected as model compounds for the study of the mechanism of the process.

Experimental results

A detailed examination was made of the progress in time of the transformations of butane-1,3-diol (Table I) and pentane-1,4-diol (Table II) on the action of acetyl chloride. In order to study the mechanism of the reaction, (+)-butane-1,3-diol was reacted with acetyl chloride.

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Table I

Variation of the product distribution during the reaction of butane-1,3 diol and acetyl chloride as a function of time

	Product distribution (%) at various times							
	0* hr	1 hr	2 hr	3 hr	4 hr	6 hr	24 hr	25 hr
mono- and diacetates	79	66	57	50	44	41	32	27
chloroacetates	20	33	42	49	54	54	55	59
chlorohydrins	1	1	1	1	2	5	13	14
monoacetates	30	23	17	17	17	33	26	18
diacetates	70	77	83	83	83	67	74	82
$CH_3-CH(OAc)-CH_2-CH_2Cl$	70	70	70	67	67	67	66	64
$CH_3-CH(Cl)-CH_2-CH_2OAc$	30	30	30	33	33	33	34	36
$CH_3-CH(OH)-CH_2-CH_2Cl$	66	67	68	69	70	75	80	87
$CH_3-CH(Cl)-CH_2-CH_2OH$	34	33	32	31	30	25	20	13

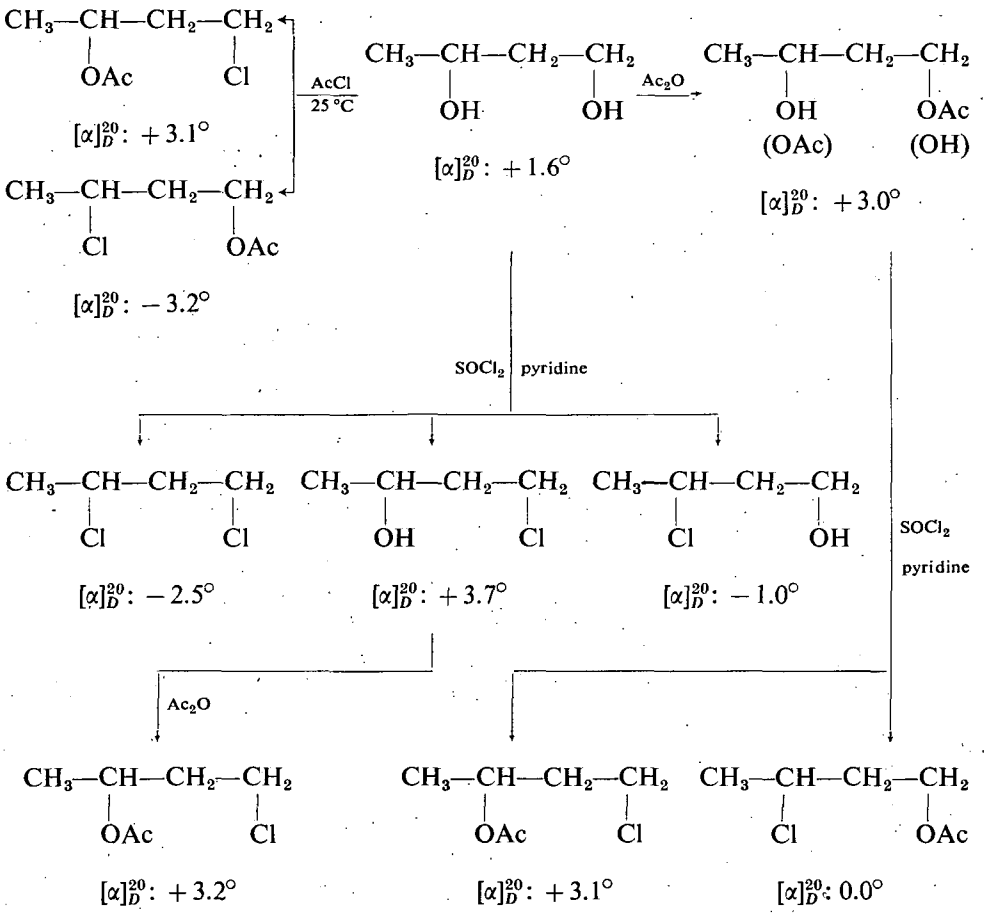
* The time when the total amount of acetyl chloride has been added dropwise to the diol.

Table II

Variation of the chloroacetate isomer distribution as a function of time in the reaction between pentane-1,4-diol and acetyl chloride

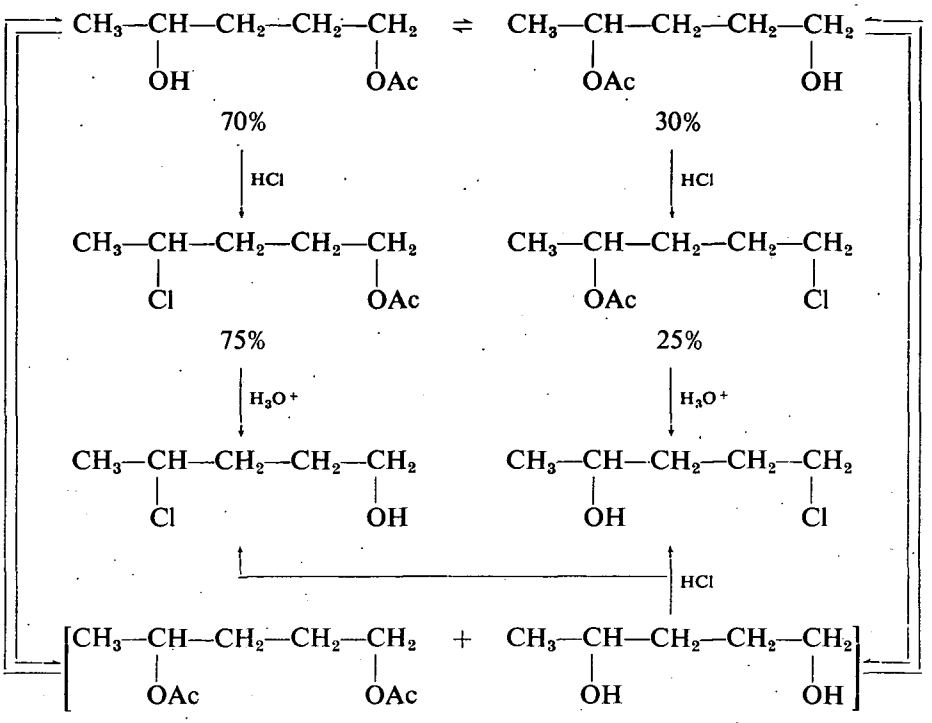
	Isomer distribution (%) at	
	0 hr	24 hr
$CH_3-CH(OAc)-CH_2-CH_2-CH_2Cl$	25	50
$CH_3-CH(Cl)-CH_2-CH_2-CH_2OAc$	75	50

The experimental results may be summarized by the following reaction-scheme:

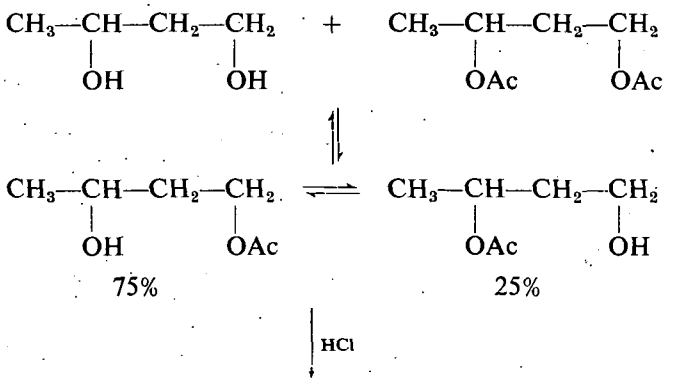


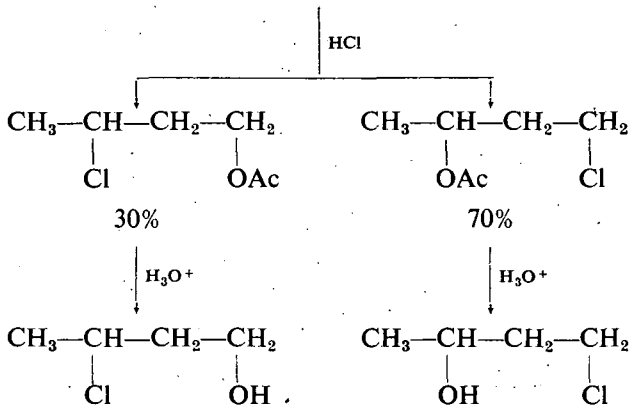
Discussion

It can be seen from the experimental data that the final chloroacetate isomer ratios resulting from the action of acetyl chloride are similar in the cases of butane-1,3-diol and pentane-1,4-diol. By following the reaction in time, however, it can be established that in these cases we are concerned with mixtures practically at equilibrium, and thus the above similarity is to be expected. On the other hand, the initial isomer ratios substantially differ from each other. For the pentane-1,4-diol the initial isomer ratio indicates that the process is undoubtedly an S_N2 type reaction. On the basis of the material reported in the preceding paper, the process can be described as follows:

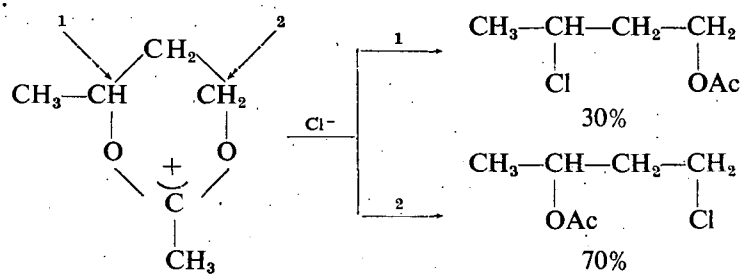


In the case of butane-1,3-diol the situation is completely different. The initial chloroacetate ratio does not correspond at all to the product ratio expected for an S_N2 type reaction from the consideration of the given monoacetate equilibrium ratio. In addition, the reaction here proceeds at room temperature too, in spite of the fact that an S_N2 type reaction would not be expected to take place under such conditions [2]. Therefore, the reaction proceeds in accordance with some other reaction type. Under the given conditions chlorohydrins can be formed only by the desacetylation of the chloroacetates:

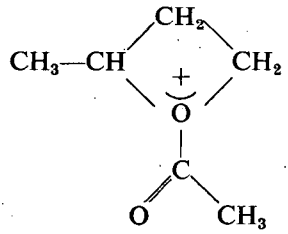




For the substitution reactions of 1,2-diol monoacetates with HCl, BOSCHAN and WINSTEIN [3] first assumed and then convincingly proved the formation of a five-membered cyclic acetoxonium cation. Later evidence was found for the existence of the six-membered cyclic acetoxonium cations, too [4, 5]. As a consequence of the similarity between the 1,2-and 1,3-diols [1], also in the case of the 1,3-diol monoesters the formation of a six-membered cyclic acetoxonium cation as a transition state may be assumed. The initial isomer ratio found may be explained on the basis of this assumption, since the attack of the chloride anion from direction 2 is more probable:



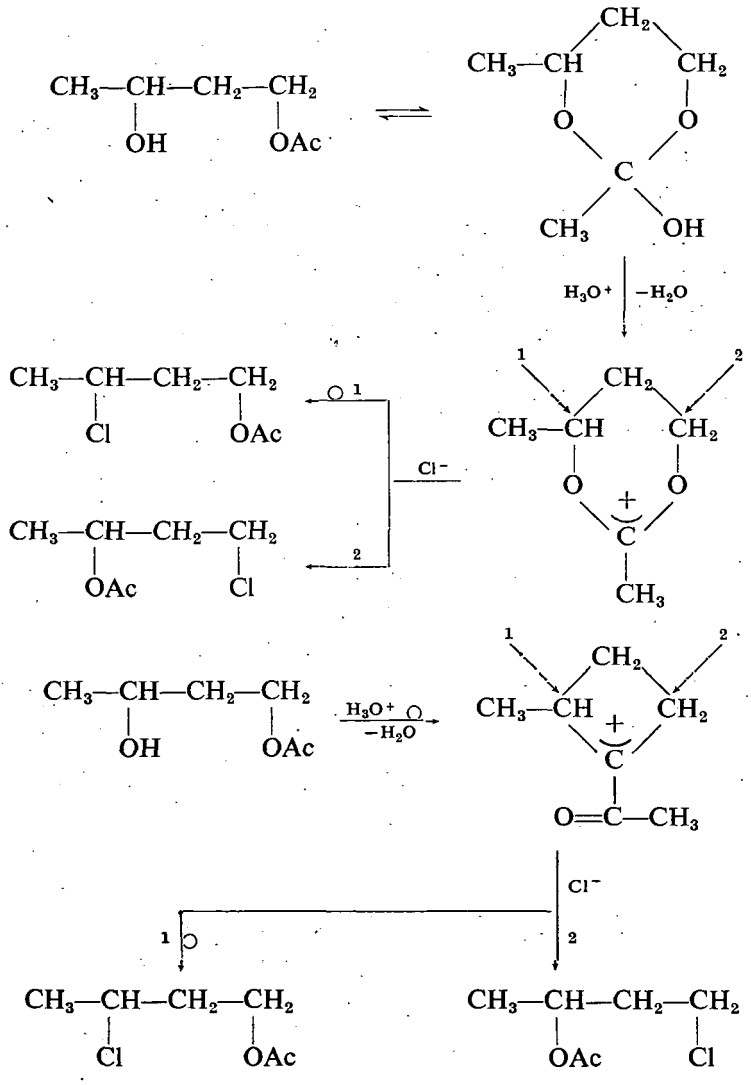
The mechanism of the transformation of butane-1,3-diol on the action of acetyl chloride was also studied by SEARLES *et al.* [6], who assumed an oxethane type transition state:



Their assumption was based on the fact that butane-1,3-diol and 2-methyloxethane give products of identical composition with acetyl chloride. According to our experimental data, in these cases we are concerned with equilibrium chloroacetate

mixtures, and thus the similar isomer ratio to be expected. It follows that it is not possible to draw far-reaching kinetic conclusions from the experimental fact observed by SEARLES *et al.*

A means of discriminating between the two alternatives is provided by the fact that the two reaction mechanisms involve different stereochemical consequences. In the case of the six-membered cyclic acetoxonium cation assumed as transition state, the configuration of the 1-chloro-3-acetoxybutane will agree with the configuration of the starting diol, whereas in the case of the mechanism assumed by SEARLES *et al.* the configuration of the 1-acetoxy-3-chlorobutane will be the same as that of the starting diol:



As we have already described, both monoacetate isomers are formed in the acetylation of the diols. In the case of the mechanism assuming the acetoxonium cation, there are no stereochemical requirements involved. In the case of the mechanism put forward by SEARLES *et al.*, 1-acetyl-2-methyloxethanes of opposite configurations are formed from the two monoacetates. However, with regard to the fact that the amount of 1-acetoxybutane-3-ol is three times that of the other monoacetate isomer and that the rate of its further transformation is probably greater than that of the other isomer, the presence of 3-acetoxybutan-1-ol makes the evaluation somewhat more difficult by the decrease of the final optical activity, but essentially does not prevent it.

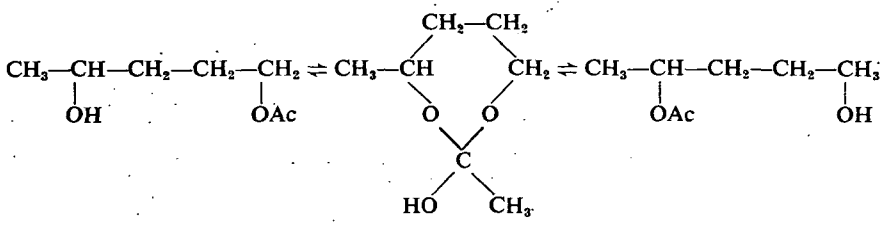
When (+)-butane-1,3-diol is reacted with acetyl chloride, the product is (+)-1-chloro-3-acetoxybutane. According to LUCAS and GOULD [7], in the case of 1,2-chlorohydrins reacting with thionyl chloride in pyridine, Walden inversion takes place. It may be assumed that the process occurs in a similar way in the case of 1,3-diols and their monoacetates too.

The configuration of the 1-chlorobutan-3-ol prepared from (+)-butane-1,3-diol with thionyl chloride agrees with the configuration of the diol, since during the reaction there was no change on the optically active carbon atom.

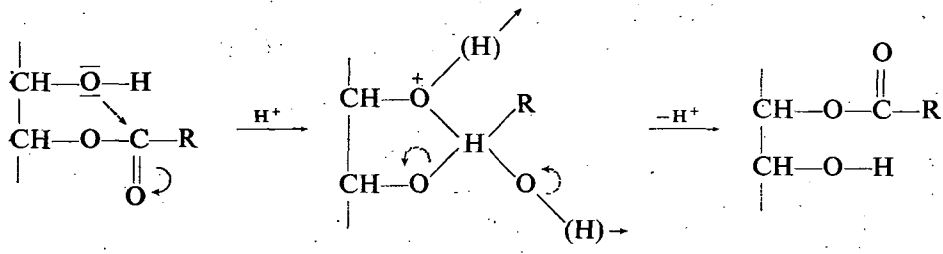
As already described above, the 1-chloro-3-acetoxybutane obtained in the acetylation of 1-chlorobutan-3-ol is dextro-rotatory. The same result is obtained by the measurement of the optical activity of the 1-chloro-3-acetoxybutane prepared by the reaction of thionyl chloride with the monoacetate mixture resulting from the acetylation of (+)-butane-1,3-diol. It follows from these results that the configuration of the (+)-1-chloro-3-acetoxybutane obtained from the (+)-butane-1,3-diol is the same as that of the starting diol. This fact indicates that the five-membered cyclic acetoxonium cation transition state assumed by BOSCHAN and WINSTEIN in the reactions of 1,2-diol monoacetates with HCl may also be employed in reactions of a similar type for 1,3-diol monoacetates, with the assumption of a six-membered cyclic acetoxonium cation as transition state. When the 1,3-monobenzoates react with HCl, presumably in a similar way, the intermediate transition state is a six-membered cyclic benzoxonium cation. The di-primary 1,2- and 1,3-diols behave similarly to the primary-secondary 1,2- and 1,3-diols, with the difference that the transition state for these diols is an acyloxonium cation of symmetrical structure.

The fact that in the reaction of pentane-1,4-diol with acetyl chloride the process does not occur by the above mechanism but by an S_N2 type reaction indicates that the formation of the seven-membered cyclic acetoxonium cation is not possible under the experimental conditions used. This finding is in complete agreement with the conclusion of PAULSEN and BEHRE [8] that in the reaction of 1,4-diacetoxybutane or *cis*-1,4-diacetoxycyclohexane with HF, a seven-membered acetoxonium cation is probably not formed.

In an earlier paper [1] it was described that in acidic medium the equilibrium between the monoacetates of pentane-1,4-diol is established extremely rapidly by means of intramolecular acyl migration. It was assumed by FISCHER [9] that acyl migration reactions of this type proceed *via* intermediate states with cyclic orthoacetate structures:



However, if such a type of orthoacetate intermediate containing a seven-membered ring were to be formed, then protonation would certainly take place, followed by the formation of a seven-membered cyclic acetoxonium cation by the elimination of water, since no fundamental difference can be assumed in the occurrence of these reaction steps between the six- and seven-membered cyclic orthoacetates. The formation of the seven-membered cyclic acetoxonium cation could, however, not be detected, and so this is a new proof in favour of acyl migration reactions proceeding *via* a cyclic transition state [10]:



In addition to elucidating the pH-dependence of the acyl migration reaction [11], this conception also provides a possibility for the explanation of the phenomenon observed in the case of pentane-1,4-diol. The failure of the seven-membered acetoxonium cation to form is caused by the thermodynamically unfavourable nature of the formation of the seven-membered cyclic orthoester intermediate, while at the same time the acyl migration may proceed *via* a transition state of similar structure.

Experimental

(+)-*Butane*-1,3-*diol* was prepared by the fermentation reduction of aldol [12]. B.p. (4 mm Hg): 90—91 °C; n_D^{24}: 1.4412; $[\alpha]_D^{20}$: +1.6°.

Reaction of diols with acetyl chloride

(a) The process was followed in time by the method described in the previous paper [1].

(b) The (+)-butane-1,3-diol was reacted at 25 °C with acetyl chloride as described previously [1]. The product was separated by preparative gas-chromatography, and the optical activities of the two chloroacetate isomers were measured.

Reactions with thionyl chloride

The reactions with thionyl chloride were carried out in pyridine using the method of [7].

(a) (+)-Butane-1,3-diol was reacted with thionyl chloride. The product was separated by preparative gas-chromatography, and the optical activities of the two chlorohydrins and the 1,3-dichlorobutane were measured. The 1-chlorobutan-3-ol was acetylated with acetic anhydride in pyridine, and the optical activity of the product was measured.

(b) (+)-Butane-1,3-diol was acetylated with acetic anhydride in pyridine. The optical activity of the product was measured, and the monoacetate mixture was then reacted with thionyl chloride as described above. The product was separated by preparative gas-chromatography, and the optical activities of the chloroacetate isomers were measured.

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ХИМИЧЕСКИЕ ПРЕВРАЩЕНИЯ ДИОЛОВ И ЦИКЛИЧЕСКИХ ЭФИРОВ. XXXIV. МЕХАНИЗМ РЕАКЦИЙ ВЗАИМОДЕЙСТВИЯ ДИОЛОВ С ХЛОРАНГИДРИДАМИ ОРГАНИЧЕСКИХ КИСЛОТ

Ф. Нотейс, М. Барток и В. Ремпорт

Изучался механизм реакции взаимодействия диолов с хлорангидридом уксусной кислоты и, в особенности, вторая стадия реакции — замещение гидроксильной группы моноацетатов хлоридом. Установлено, что ди-первичные- и первично-вторичные 1,3-диолмоноацетаты — аналогично 1,2-диолмоноацетатам — проходят через промежуточную стадию образования ацетоксоний катиона. Моноацетаты 1,4-диолов взаимодействуют с соляной кислотой по типу S_N2 реакций. Это обстоятельство показывает, что в изученных условиях семичленный циклический ацетоксоний катион не образуется. Вследствие, этого, тот факт, что у 1,4-диолмонацетатов в кислой среде происходит переход ацильных групп, является дополнительным доказательством представления о наличии циклического промежуточного состояния при реакции миграции ацильной группы.